Summary of the Fifth
Comparative Medicine Resource Directors Meeting
October 6-7, 2004

Sponsored by:
The University of California at Davis
Davis, CA

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National Center for Research Resources
Bethesda, MD

AND

Summaries of Satellite Meetings:
Mutant Mouse Regional Resource Centers Meeting - October 7, 2004
Chimpanzee Resource and Sanctuary Directors Meeting - October 7, 2004

Introduction

Dr. Stephen Barthold of the University of California at Davis was awarded a conference grant that supported the Fifth Comparative Medicine Resource Directors Meeting held on October 6-7, 2004, in Bethesda, Maryland. Selected Principal Investigators (PIs) were invited to attend if they held resource-related grants or contracts from the Division of Comparative Medicine (DCM), National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH) and the Department of Health and Human Services. The meeting provided a forum to highlight activities of the DCM-supported resource centers and to exchange additional information. The roster of invited attendees included the PIs of NCRR-supported centers funded by contracts, P40, U24, and U42 grant mechanisms, as well as grantees who have resource-related projects funded via the R24 mechanism. Additional attendees included members of various groups that held satellite meetings in Bethesda during this same period. These groups included attendees from the Mutant Mouse Regional Resource Centers (MMRRC) Meeting, and the NIH Chimpanzee Resource and Sanctuary Directors Meeting, held just after the main meeting.

Main Meeting Agenda

Wednesday, October 6, 2004: Dr. Barthold welcomed the attendees. Dr. Judith Vaitukaitis, Director of NCRR, also welcomed the attendees and delivered an address on the 2004-2008 Strategic Plan: *Challenges and Critical Choices*. Dr. Jonathan Pollock,

Chief of the Genetics & Molecular Neurobiology Research Branch of the National Institute of Drug Abuse, NIH, then discussed the history and requirements of the NIH Data and Model Sharing Plans. Drs. Franziska Grieder and John Harding, of the DCM at NCRR, then presented an *Overview of DCM Resources* and an *Introduction of New DCM Resources* that were funded since the original meeting agenda had been prepared.

Thirteen PIs from various DCM-funded resources gave 10-minute overviews of their resources on either Wednesday or Thursday. These included the following resources that were funded or significantly modified since the last Resource Directors Meeting in 2002:

The Neurogenetics and Behavior Center (Dr. Peter Holland, Johns Hopkins University, Baltimore, MD)

The Yeast Genetic Resource Center (Dr. Jianlong Zhou, American Type Culture Collection, Manassas, VA)

Development of a Primate Genomics Resource (Dr. Michael G. Katze, University of Washington, Seattle, WA)

The Genetic Mapping Resource for Common Mammalian Diseases (Dr. Leslie Lyons, University of California, Davis, CA)

Construction of a Targeted Rhesus Macaque Microarray (Dr. Robert Norgren, University of Nebraska Medical Center, Omaha, NE)

The Viper Resource Center (Dr. John C. Perez, Texas A&M University, Kingsville, TX)

Preparation and Distribution of Adult Stem Cells (Dr. Darwin J. Prockop, Tulane University, New Orleans, LA)

The National Swine Research and Resources Center (Dr. Lela Riley, University of Missouri, Columbia, MO)

The *Drosophila* Genomics Resource Center (Dr. Justen Andrews, Indiana University, Bloomington, IN)

New Vertebrate Model Organism cDNA Libraries (Dr. Bruce Blumberg, University of California, Irvine, CA)

A Facility for *S. pombe* Microarrays (Dr. Bruce Futcher, State University of New York, Stony Brook, NY)

A Resource for Nonhuman Primate Immune Reagents (Dr. Francois Villinger, Emory University, Atlanta, GA)

Genome Resources for Model Amphibians (Dr. Stephen Randal Voss, University of Kentucky, Lexington, KY)

For 1-1/2 hours per session, attendees organized into four Working Groups:

- Group 1 - Responding to the NIH Data and Model Sharing Plans
- Group 2 - Responding to the NCRR Strategic Plan
- Group 3 - Intellectual Property and Technology Transfer
- Group 4 - Unification and Linkage of Databases for Resources

The proceedings of these working groups are described below.

On Wednesday evening, Dr. William Morton of the University of Washington gave the Keynote Address on "The Development and Challenges of the National Primate Research Centers Program."

Thursday, October 7, 2004: The second day of the main meeting commenced with Dr. Michael Marron, Director of NCRR's Division for Biomedical Technology Research and Research Resources, giving a detailed presentation on the Biomedical Information Research Network (BIRN). Dr. William Watson of DCM then informed the attendees about DCM-funded, Specific Pathogen Free Nonhuman Primate Resources. Dr. Raymond O'Neill of DCM presented an overview of the NCRR Chimpanzee Management Program and the chimpanzee research and reserve facilities funded by NCRR. Dr. Linda Brent, President of the Chimp Haven, Inc. Board of Directors in Shreveport, LA, provided information to attendees regarding the NCRR-funded Chimpanzee Sanctuary Program.

The main meeting concluded with discussions of the Sixth Comparative Medicine Resource Directors Meeting, scheduled in Seattle in 2006. A discussion ensued regarding meeting content, most relevant workshop topics, and the time to be allotted to various agenda items. Some attendees requested that more time be reserved for discussions in addition to the formal presentations. Some attendees also requested that substantial background material for the workshops be e-mailed to the attendees prior to the meeting. Because the participation of NIH staff—in addition to DCM staff—was very helpful in this fifth meeting, it was suggested that videoconferencing be explored as a way to involve non-DCM NIH staff in the 2006 Seattle conference. The Conference Grant's Steering Committee membership was discussed, and its composition—proposed by Dr. Barthold—was agreed upon by consensus.

Additional feedback from the DCM community should be directed to the Director of DCM, NCRR via telephone at 301-435-0744, via fax at 301-480-3819; Dr. Barthold, PI of the conference grant; or Dr. William Morton at the University of Washington. Following adjournment of the main meeting on October 7, two additional satellite meetings were held: the MMRRC Group Meeting, and the NIH Chimpanzee Resource and Sanctuary Directors Meeting.

Reference: NCRR DCM

Reports of the Four Working Groups

Attendees were free to choose which Working Group to attend during each of the two extensive sessions on Wednesday. The designated leaders coordinated the discussions and reported summary remarks to all attendees on Thursday. Summaries of the Working Group discussions appear below.

Working Group 1 - *Responding to the NIH Data and Model Sharing Plans*
Dr. Lela Riley (Leader)
University of Missouri
Columbia, MO

MODEL SHARING

The NIH Policy on Sharing of Model Organisms for Biomedical Research, issued May 7, 2004, was generally well received. Most attendees thought that the statement included in the plan should be somewhat general. The existing sample templates will be helpful to applicants as they submit applications.

However, concerns were noted about the following:

1. What will be the source of funds to pay for archiving animal models? In which cases should investigators request funding in the initial application rather than as an administrative supplement? If investigators request funding to send models to a resource center, should this portion of the funding be excluded from indirect cost calculations for the parental grant, since it is essentially a subcontract?
2. How will existing resource centers manage the potential of being overwhelmed by the number of incoming models?
3. Will the resource centers be able to ensure that shared models are of the expected and appropriate genotype—free of infectious pathogens?

The following suggestions were made:

1. Existing resource centers could supply sample templates that provide language and costs for submitting animals to the centers. These templates would assist new research investigators with this part of the application.
2. The PHS 398 instructions should be revised to provide applicants with specific instructions (similar to the instructions for the Vertebrate Animal section) to address this new component of the application. Some attendees believed it would be helpful to revise the budget page, thereby making "Sharing" a specific budget category.
3. Address the need to identify mechanisms to further educate applicants and other NIH Institute and Center personnel about existing resource centers, and the benefits of using these centers for distribution (e.g., their cost-effectiveness and

ability to provide high-quality model organisms of verified genotype, phenotype, and health status to the community).

DATA SHARING

Similar to Model Sharing discussed above, Data Sharing is not a new concept. Therefore, the Final NIH Statement on Sharing Research Data—applied first in October 2003—will reinforce the existing concept that data obtained with public funds should be made widely available.

Several recommendations regarding implementation were discussed:

1. The consensus of the attendees was that only final data, which have been peer-reviewed, should be made widely available.
2. Existing resource centers could and should play a role in making data available.

A brief discussion was held regarding placing published scientific articles in a NIH database. (See NOT-OD-04-064, Notice: Enhanced Public Access to NIH Research Information.)

Working Group 2 - *Responding to the NCRR Strategic Plan*
Dr. Julia Hilliard (Leader)
Georgia State University
Atlanta, GA

The attendees discussed issues related to NCRR resources in view of NCRR's 2004-2008 Strategic Plan: *Challenges and Critical Choices*. The discussion emphasized how the individual centers and other NCRR stakeholders can enhance the visibility and knowledge of NCRR-supported resources both within the NIH and by the largely untapped public constituency. The consensus ideas came from an underlying premise that NCRR resource centers are often under-recognized as cost-saving resources made available to researchers. The Strategic Plan may be used as a basis for disseminating information about these "national treasures," as major contributors to global research initiatives.

The discussants identified a number of issues that should be addressed with NCRR staff in order to facilitate successful implementation of the NCRR Strategic Plan. These include:

1. Public advocacy for NCRR resources.
2. Creating uniform formats for preparing resource center data that can be used by anyone planning or preparing an NIH grant application.
3. The need for model systems for organizing data and information. Possible examples include the Primate InfoNet, various National Science Foundation-funded programs, BIRN, and the various efforts of the NIH National Center for Biotechnology Information, but applied across phylogenies.

4. Interactive resource development and use of a Web site for presentation of the integrative aspects of resources.
5. Various mechanisms for highlighting the accomplishments and capabilities of the NCRR resource centers, including: publications, databases, number of users, numbers of citations, high-risk projects carried out in resource centers, interdisciplinary research and instrumentation, educational missions and advances, and others.
6. The discussants also believed that some new funding mechanisms may help facilitate implementation of the NCRR Strategic Plan as well as generally advance the mission of the NIH. These include: new funding for postdoctoral training and associated Ph.D. graduate programs specifically involving animal-based research and collaborations with veterinarians; greater utilization of National Research Service Award grants and pre-veterinary research opportunities; and new Requests for Applications to help integrate research information.

Finally, the discussants emphasized the fact that, in many cases, NCRR resources impact research on a global scale.

Working Group 3 - *Intellectual Property and Technology Transfer*
Dr. James Geistfeld (Leader)
Taconic Farms, Inc.
Germantown, NY

The attendees discussed several concerns highly relevant to DCM-funded resources and research investigators:

1. The need and time required for researchers to comply with patent requirements have become exceedingly complex, sometimes costly, and time consuming. This causes much frustration for the research community. People left this short session with more questions than answers regarding this issue.
2. Adherence to patent requirements adds significant costs to research. It is not unusual for researchers to pay royalties on four or five patents to obtain and use a single mouse model. This adds greatly to cost accounting. It was thought that most of these funds are being distributed from one university to another.
3. The costs required to comply with patent requirements affect many fields of research: various vertebrate and invertebrate animals, yeast, cell lines, and processes. Often, researchers don't know about all of the patents that underlie the models they are accessing, but researchers are still liable if patent infringement occurs.
4. There are a variety of "model" Material Transfer Agreements (MTAs), Simple Letter Agreements, or Uniform Biological Material Transfer Agreements available; however, the various "offices of technology transfer" at universities often receive proposed MTAs, cannot reach them for review for months, and then change them in either minor or major ways, which necessitates re-review by the other involved parties. It was suggested that "standard" MTAs could be strongly

recommended in language appearing in the Notices of Grant Awards for P40 and other grants from NIH. If this increased compliance with patent requirements, then the various institutional offices of technology transfer may begin to accept the standard MTAs suggested by NIH. (Please see NIH-recommended MTAs and Additional Documents and Links About Sharing Model Organisms and Sharing of Model Organisms and Related Resources: Frequently Asked Questions.)

5. NIH staff members Lili Portilla and J. P. Kim are available to help resource directors with issues associated with intellectual property. In addition, good MTA models are available from the MMRRC and the Zebrafish Information Network.
6. The group asked that NIH conduct more outreach to the university technology transfer departments. Some attendees thought that some university technology transfer departments might be more responsive to NIH comments and suggestions than to the Principal Investigators at their universities.
7. Adherence to patent requirements can be problematic. One example is the technology for making transgenic mice known as Cre-lox. Parts of the patents for this technology are apparently controlled by Bristol Myers and other parts by Dupont. The MMRRC does not send these models to the two centers with commercial operations but rather to the two nonprofit centers due to potential legal issues.
8. There was general concern about breaking the law and liability. Generally, the patent has to be enforced, and it is usually not worth the negative publicity and small amount of money for most patent holders to pursue most non-commercial entities, although this should not be relied upon.
9. A requesting investigator can be covered by a license from one organization that may have other necessary cross-licenses for the procedure that are not obvious. If these cross-licenses do not pass through to the requesting investigator, the requesting investigator is probably required to also obtain the required licenses from the other patent holders, who may be difficult to fully identify.

Working Group 4 - *Unification and Linkage of Databases for Resources*
Dr. K.C. Kent Lloyd (Leader)
University of California
Davis, CA

There is a need for a broad and deep Web-based portal to serve as a first-stop access point to databases available to anyone interested in biomedical and behavioral research. However, achieving this goal is neither within the foreseeable future nor within the scope of this working group. Instead, it represents a vision that can be attained through careful, precise, and practical planning and implementation. This portal is envisioned as an extension of existing Web pages such as those listed in the NCRR Comparative Medicine Research Resources Directory and on the NIH Model Organisms for Biomedical Research page.

The most appropriate starting point may be a Web page hosted and maintained by the NIH/NCRR that serves as a model for further development. The opening page would list a limited number (~12) of the organism resources most commonly used for research

today. Clicking on an organism would link to a second page listing a few categorical topic areas; under each would be listed known associated databases. Clicking on any of the database URLs would link directly to the home page of the individual database.

This plan would serve as a model that could be implemented rather quickly so as to test its effectiveness and would encourage feedback from users to guide further development. While the model itself can change as well, the most likely evolutionary changes that are to be expected over time will be the addition of more organism resources and more databases within each of the categorical topic areas.

A simple example of the hierarchical structure is the following:

Organism:

- Human resources
- Nonhuman primate resources
- Rodent resources, etc.

Categorical Topic Areas (as a subtopic under each organism listed above):

- Anatomical structure
- Organ systems
- Genes/gene expression
- Technologies, etc.

Databases and Resources (as a subtopic under each categorical topic area listed above):

- Links to many individual Web sites

In order for such a Web portal to have greatest value, the site must be credible, reliable, comprehensive, and up to date; furthermore, it should not be seen as competitive with existing Web portals, burdensome, or unmanageable. Conceptual development and design should arise from a working group of stakeholder academic scientists who meet to draft the critical questions that such a site must serve to answer for any potential user. Finally, the attendees recommended that databases be hosted and maintained in an uninterrupted fashion, thereby requiring it to be either institutionally supported, or specifically funded by a government agency, to ensure sustainability.

Summaries of Satellite Meetings

Mutant Mouse Regional Resource Centers (MMRRC) Group
Thursday, October 7, 2004
Dr. Franziska Grieder (Leader)
DCM, NCRR
Bethesda, MD

The MMRRC Coordinating Committee (CC) used this conference as a face-to-face meeting to replace the monthly teleconference for October. After Lili Portilla of the National Heart, Lung, and Blood Institute (serving as a technology transfer consultant to NCRR) discussed related information, CC members decided that they did not see a need to register the newly designed MMRRC logo as a trademark.

Regarding a possible MMRRC bulletin or newsletter, the attendees decided that each of the five centers would rotate writing an article for the quarterly MMRRC newsletter. The newsletter will also list newly available mouse strains as well as newly admitted strains to the MMRRC.

CC members also discussed the use of 129/Sv and associated substrains of ES cells, or C57BL/6 ES cells, or a hybrid of 129/S and B6 ES cells. After some considerable discussion, they decided to not endorse either the B6 or 129 backgrounds.

The next discussion points focused on reviewing the status of action items discussed at the annual MMRRC meeting in April 2004:

1. Lili Portilla is working with the Informatics Coordinating Center (ICC) and the technology transfer policy subcommittee on both policy for distribution to for-profit requesters and updating the material transfer agreement for the MMRRC.
2. The ICC is improving the MMRRC catalog (e.g., listing the MMRRC strains accepted, but not yet available for distribution).
3. The Health and Genetics Committee is working on posting new Standard Operating Procedures.
4. The Public Relations Committee will be working on a Customer Satisfaction Survey.

Last, new strain submissions were reviewed and assigned to centers.

Reference: MMRRC

NIH Chimpanzee Resource and Sanctuary Directors Meeting
Thursday, October 7, 2004
Dr. Raymond O'Neill (Leader)
DCM, NCRR
Bethesda, MD

The group discussed many issues. First, a brief status report and discussion was held on two topics:

1. Current NCRR-funded chimpanzee facilities
2. The demographics of US chimpanzees and their support/ownership

This update was followed by a discussion regarding animal records issues led by the representative from the International Species Information System (ISIS). It was agreed

that DCM staff would send each of the major chimpanzee facilities a request by e-mail to assemble hard data regarding potential short- and long-term national chimpanzee breeding capabilities.

A brief characterization of the chimpanzees at the Alamogordo Primate Facility was presented. At this time, there are approximately 30 chimpanzees that test positive for Hepatitis C Virus by polymerase chain reaction technologies; they are sufficiently healthy to be transferred to sites that conduct peer-reviewed funded, long-term invasive research protocols.

An update on the PL 106-551 Chimpanzee Health Improvement, Maintenance, and Protection (CHIMP) Act as it relates to the Chimpanzee Sanctuary contract was presented. This update included a discussion of expected timelines for construction and receipt of the first chimpanzees expected to arrive in January 2005, as well as additional ones expected to arrive later in 2005. The Regulations for standards applying only to the NCRR-supported sanctuary (but not the NCRR-supported research facilities or privately funded sanctuaries) were under review in October 2004 for governmental approval at multiple levels.

Reference: NCRR's NIH Chimpanzee Management Program

ROSTER

Fifth Comparative Medicine Resource Directors Meeting and Satellite Meetings: Mutant Mouse Regional Resource Centers Meeting Chimpanzee Resource and Sanctuary Directors Meeting

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